REMARKS

Claims 1-30 and 34-64 are currently pending, with claims 1-30 and 52-56 under consideration (claims 34-51 and 57-64 having been withdrawn by the Examiner as drawn to non-elected subject matter). Claims 1, 9-11, 13, 15-17, 52, and 54 are amended by the present communication. None of the subject amendments adds new matter as all are supported by the specification at, for example, paragraphs [0032] and the claims as originally filed. In view of these amendments, claims 12 and 53 are canceled herein without prejudice or disclaimer. Upon entry of the present amendment, claims 1-11, 13-30, 52, and 54-56 and will remain pending and under consideration.

Rejection Under 35 U.S.C. §102, or in the Alternative Under 35 U.S.C. §103

Claims 1-9, 18, 25 and 56 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by or, in the alternative, under 35 U.S.C. §103(a) as allegedly obvious over Thomson *et al.* (*Science* 282:1145-1147, 1998; hereinafter "Thomson"). Applicants respectfully traverse the rejection as it might apply to the pending claims for at least the reasons that follow.

The present invention is based on the discovery that adult human cells can be used as feeder cells for growing continuous cultures of undifferentiated pluripotent human embryonic stem (hES) cells. In particular, the specification provides that "the hES cells passaged in culture using the disclosed compositions and methods have maintained a diploid karyotype and have remained in an undifferentiated state after continuous culture and many passages" (specification at paragraph [0008]). Accordingly, claim 1, as presently amended, is directed to isolated undifferentiated pluripotential hES cells, which are passage 4 or higher, have a diploid karyotype, express Oct-4 and do not express stage-specific surface antigen-1 (SSEA-1), and exhibit a dependence on adult human feeder cells or a cell-maintaining product thereof for maintenance in culture in an undifferentiated state for 4 or more passages.

The Examiner asserts that Thomson teaches isolated hES cells that have a normal, diploid karyotype and are passaged for at least 32 passages and that all hES cells require, as an inherent property, either a feeder cell layer or feeder cell conditioned media. However, contrary to the Examiner's assertion, Thomson does not teach all of the elements of the claims as presently amended. Specifically, Thomson fails to teach undifferentiated hES cells that 1) express Oct-4 and do not express stage-specific surface antigen-1 (SSEA-1), and 2) and exhibit dependence on adult human feeder cells or an hES cell-maintaining product of the adult human feeder cells for maintenance in culture in an undifferentiated state.

Thomson provides a method for isolation and culture of embryonic stem cell lines derived from human blastocysts. In particular, Thomson provides methods for isolating and passaging undifferentiated ES cells on mouse embryonic fibroblasts, but that "the ES cells differentiated when cultured in the absence of mouse embryonic fibroblast feeder layers" (Thomson at p. 1146, col. 1, 2nd full paragraph). Thomson provides no teaching with regard to the requirement that the cells exhibit a dependence on adult human feeder cells or a cell-maintaining product thereof for maintenance in culture in an undifferentiated state for 4 or more passages.

With respect to claims 18, 25, and 56, the cells embraced by these claims were obtained by the methods of claims 17, 24, and 52, respectively. As such, Applicants respectfully submit that the claimed cells are novel and non-obvious in view of Thomson because Thomson does not teach the methods by which these cells were obtained.

Applicants submit that the courts have recently found that a product-by-process limitation can distinguish a claimed product over a prior art product made by a different process. In particular, the court in *Abbott Laboratories and Astellas Pharma, Inc. v. Sandoz, Inc., Sandoz GMBH, Teva Pharmaceuticals USA, Inc. and Teva Pharmaceutical Industries, Ltd., Ranbaxy Laboratories, Ltd. And Ranbaxy, Inc., and Par Pharmacuetical Companies, Inc. and Par Pharmaceutical* (Fed. Cir. 2009), took the opportunity "to clarify en banc the scope of product-by-process claims by adopting the rule in *Atlantic Thermoplastics*." The Supreme Court has long emphasized the limiting requirement of process steps in product-by-process claims. Based

on Supreme Court precedent and the treatment of product-by-process claims throughout the years by the PTO and other binding court decision, this court now restates that "process terms in product-by-process claims serve as limitations in determining infringement." *Atlantic Thermoplastics Co. v. Faytex Corp.*, 970 F.2d 834 (Fed.Cir.1992). This holding follows this court's clear statement in *In re Thorpe* that "product by process claims are limited by and defined by the process." 777 F.2d at 697. To the extent that *Scripps Clinic* is inconsistent with this rule, this court hereby expressly overrules *Scripps Clinic* (*Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d. 1565 (Fed. Cir. 1991).

Applicants respectfully submit that claims 18, 25, and 56, distinguish over Thomson because Thomoson provides no disclosure as to the specific method steps presently required in claims 17, 24, and 52. Accordingly, Thomson does not teach all of the elements of claims 18, 25, and 56.

Based on the reasons set forth above it is respectfully submitted that Thomson does not anticipate or render obvious the present claims. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

Rejections under 35 U.S.C. §103

Claims 10-17, 19-24, 26-30, and 52-55 stand rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Mitalipova *et al.* (U.S. Patent Publication No. 2005/003748; hereinafter "Mitalipova") and Thomson (supra) in view of McIntosh et al. (PCT Publication No. WO 00/029001; hereinafter "McIntosh"). Applicants respectfully traverse the rejection as it might apply to the pending claims for at least the reasons that follow.

The Examiner asserts that Mitalipova teaches a culture of hES cells grown on immortalized human skin fibroblasts and a method of obtaining an expanded population of undifferentiated pluripotent hES cells. The Examiner further asserts that the fibroblasts are adult feeder cells producing an ES cell-maintaining product of the supportive adult human feeder cells as well as the use of the feeder cells to produce conditioned media. The Examiner cites Thomson for allegedly teaching isolated hES cells that have a normal, diploid karyotype and are

passaged for at least 32 passages. McIntosh is cited for allegedly teaching the fibroblast cell line 1087sk and its use in preparing conditioned media. Contrary to the Examiner's assertion, the combination of Mitalipova, Thomson, and McIntosh do not disclose all of the elements of the claims.

The claims as presently amended require that the hES cell-maintaining product is a product of adult human feeder cells and comprises a fraction of conditioned medium consisting of biomolecules having a molecular mass greater than about 30 kiloDaltons. Mitalipova provides no teaching with regard to the use such a fraction of conditioned medium.

Moreover, Thomson and McIntosh cannot cure the deficiencies of Mitalipova because both are silent with regard to the use of a fraction of conditioned medium consisting of biomolecules having a molecular mass greater than about 30 kiloDaltons for culture of undifferentiated hES cells. Therefore, because the cited references taken alone or in combination fail to teach all of the elements of amended claims, a *prima facie* case of obviousness has not been established for the claims. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

CONCLUSION

In view of the foregoing amendments and the remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this case.

No fee is believed to be due in connection with this submission. However, the Commissioner is hereby authorized to charge any other fees associated with the filing submitted herewith, or credit any overpayments to Deposit Account No. 07-1896 referencing the above-identified attorney docket number.

Respectfully submitted,

Date: February 19, 2010

Lisa A. Haile, J.D., Ph.D.
Registration No. 38,347
Telephone: (858) 677-1456
Facsimile: (858) 677-1465

DLA PIPER LLP (US)
4365 Executive Drive, Suite 1100
San Diego, California 92121-2133
USPTO CUSTOMER NO. 28213